UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/458,998	12/10/99	MOORE	N

HM22/0213

MARY HELEN SEARS
THE M H SEARS LAW FIRM CHARTERED
910 SEVENTEENTH STREET NW SUITE 800
WASHINGTON DC 20006

EXAMINER	
HINES, J	
ART UNIT	**PAPER NUMBER**
1645	4

DATE MAILED: 02/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/458,998	Moore
Examiner	**Group Art Unit**
Ja-Na Hines	1645

☒ Responsive to communication(s) filed on *Dec 10, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-9* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Drawings

1. The drawings are objected to because of the reasons set forth in the attached PTOL-948. Correction is required.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The specification incorporates by reference the specification of application 09/139,720. This parent specification teaches extraction steps in examples VII and VIII which are critical or essential to the practice of the invention in the instant application, but not included in the claims is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claims 1-9 do not recite the use the O-polysaccharide antigen sample. In examples I and II of the parent application the *Legionella* bacteria antigen is a O-polysaccharide. Examples II-V of the parent application teach preparation, conjugation and coupling of the O-polysaccharide antigen to the chromatographic column. Example VI of the parent application teaches affinity purification of antibodies to the O-polysaccharide antigen. However, all of the claims of the instant application recite the use of an antibody produced from purified antigen-specific chromatographic affinity column. These antibodies are specific for epitopes on the O-polysaccharide, and not to any other epitopes found on the outer membrane or any other portion of *Legionella pneumophila* serogroup I. The claims do not recite a preparation or pre-treatment step to make a O-polysaccharide antigen within the sample possibly containing *Legionella*. If the appropriate antigen (i.e. the O-polysaccharide) is not present, then the antigen specific Legionella antibodies will not bind and will not detect the presence of *Legionella*.

4. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is directed to assaying for the presence of *Legionella pneumophila* serogroup I, however the steps in the claims are directed to making antibodies, there are no method steps to detect *Legionella* which is critical or essential to the practice of the invention, but not included in the claims. There are no steps taught for contacting a sample containing the antigen of interest with antibody, no detection step, and no step which correlates detection of

antigen to the presence of *Legionella*. All the claims are directed to antibody purification steps and not to methods for detecting *Legionella* in an enzyme immunoassay.

5. It is unclear how the antibody of claim 1 relates to the enzyme label needed for detecting *Legionella*. There is no association or relationship between the label and the antibody, therefore it is unclear whether the label would be conjugated to the antibody and how appropriate detection can occur without a label.

6. In claim 1, abbreviations like *L. pneumophila* must be spelled out when used for the first time in a chain of claims.

7. In claim 4, Acronyms like EIA must be spelled out when used for the first time in a chain of claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-3, 5-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al.(US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832) in further view of Strosberg et al (US Patent 4,780,407). Imrich et al. (US Patent 5,415,994), teaches methods for detecting analytes in biological sample where prior to detection, extraction can occur (col.1 lines 5-10). Clinical detection of microbial pathogen in biological samples can determine accurately and rapidly infectious pathogens (col. 1 lines 23-30). Species-specific antigen of many pathogenic organisms require pretreatment prior to detect, like *Legionella pneumophila*, and it may be detected by non-serotype monoclonal antibodies after pretreatment with detergents and other reagents (col. 1-2 lines 67-3). Biological material can be obtained from patients and includes urine, serum, sputum, and pharyngeal exudates (col.3 lines 9-13). Non-patient non-biological samples may also be used (col. 3 lines 25-28). To detect *Legionella pneumophila*, a sample may be pretreated with an extraction solution (col. 4 lines 20-24). Bibulous materials such as untreated paper, nitrocellulose, derivatized nylon, cellulose and other like materials may be used along with appropriate blocking agents (col. 4 lines 56-63). The extraction method comprises inserting a swab into the extraction chamber, observing the accumulation and determining the presence or absence of analyte in the sample (col. 7 lines 50-56). The labeling zone contains a means for specifically labeling the target analyte. Immunoglobulins may be antibodies of any isotype or like fragments (col. 5 lines 15-23). The label may be soluble or particulate and may include dyed immunoglobulins binding substances such as dyes, polymers, latex beads or metallic sols (col. 5 lines 28-38). "As treated sample flows through the labeling

zone, the target analyte in the sample binds the labeled antibody thereby indirectly labeling the target analyte. The sample continues to flow into the capture zone on the matrix. A compound capable of specifically binding the labeled target analyte is immbolized in the capture zone. As sample flows into the capture zone labeled target analyte will bind the immobilized immunoglobulins thereby retaining label in the capture zone. The presence of analyte in the sample may then be determined by visual identification of label retention in the capture zone (col. 5 lines 39-52). Example 1 conjugated hors radish peroxidase as the enzyme label used for detection means.

However, Imrich et al., do not teach the use of a chromatographic column.

Cuatrecasas et al., teaches the polysaccharide matrices comprising macromolecule spacer arms for use as adsorbents in affinity chromatography techniques. Affinity chromatography techniques are used to purify various biologically active molecules and use soluble macromolecular "spacer" or "arms" to separate a polysaccharide matrix from the specific ligand to be purified (col. 1 lines 17-26). Affinity chromatography exploits the unique biological property of these proteins to bind ligands specifically and reversibly (col. 1 lines 40-43). Proteins to be purified can be passed through a column containing insoluble polymers or gel to which specific competitive ligand has been covalently attached (col. 1 lines 43-45). Proteins not displaying appreciable affinity for the ligands will pass unretarded through the column, whereas those which recognize the inhibitor will be retarded to an extent related to the affinity constant under experimental conditions (col. 1 lines 45-51). The principle uses "immunoadsorbents" for

the purification of antibodies. "In order to use the method successfully, the essential group for interaction with the molecules to be purified must be sufficiently distant from the polymer surface to minimize steric interference. Such a distance can be obtained by introducing a spacer molecule bound thereto. Since the only truly effective method available for binding various molecules to the conventional matrices.. Is by activation.... the spacer must contain a free amino group through which the binding is effective. " (col.1-2 lines 60-5). A wide variety of different spacer molecules are also taught (col 3-12). However Cuatrecasas et al., do not teach the use of water samples.

Strosberg et al., teach monoclonal antibodies to *Legionella*, a process for preparations and a method of determination. Monoclonal antibodies are made to *Legionella pneumophila* serotype I (col. 2 lines 30-355). Strosberg et al., teach immunizing a mouse with an amount of dead Legionella, and creating hybrid cells that produce the desired antibody and clone those cells (col. 1-2 lines 63-13). Monoclonal antibodies can be used to detect the presence of *Legionella pneumonphilia* antigen in the urine (col. 4 lines 10-12). The use of known antigens can be isolated and purified by affinity chromatography with the monoclonal antibodies (col. 4 lines 13-120). The antibodies to *Legionella* are particularly useful for the systematic investigation of bacteria in the ambient environment for example water and air of a hospital as much from the quantitative point of view as from the qualitative point of view (col. 4 lines 35-39). Example 5 teaches the use of simple and rapid process for the detection of Legionella bacteria in water or air.

No more then routine skill in involved in adjusting the amount of a component such as water or antibody in the claimed process to suit a particular starting material in order to achieve

the results taught in the prior art. Further, changes in concentration or other process conditions of an old process do not impart patentability unless they produce a new unexpected result.

Therefore, it would have been obvious at the time of applicants invention to detect *Legionella* in as taught by Strosberg et al., using detection methods taught by Imrich et al., where the antibodies were obtained by techniques taught by Cuatrecasas et al., because Strosberg et al., teaches the *Legionella* can be detected in water samples.

9. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al.(US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832) in view of Strosberg et al (US Patent 4,780,407) in further view of Yen et al. (US Patent 4,206,094). Imrich et al., Cuatrecasas et al., and Strosberg et al., have been discussed above, however none teach the use of finely dived gold particles. Yen et al., teaches a method for producing a biological reagent. The introduction of finely divided metals would eliminate the necessity to bind radioactive or fluorescent tags (col. 2 lines 27-30). These particles are found to bind antibodies and have application in the detection of a variety of receptors (col. 3 lines 25-30). These reagents are hydrophillic, hydrolytically stable, biocompatible, have good mechanical strength, well characterized structure, and can be systematically varied by selection of conditions (col. 3 lines 43-49). The metals are fine evenly sized materials having a uniform diameter and are electron dense heavy metals like gold (Au) (col. 6 lines 23-29).

Accordingly, no more then routine skill is required to use finely divided metallic magnetic particles as taught by Yen et al., in a method to detect *Legionella* taught by Imrich et al., Cuatrecasas et al., and Strosberg et al., because Yen et al., teaches the particles eliminate the necessity to bind radioactive or fluorescent tags and the particles are hydrophillic, stable, biocompatible and have good mechanical strength.

12. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al.(US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832) in view of Strosberg et al (US Patent 4,780,407) and in further view of Jurgens et al. Imrich et al.,Cuatrecasas et al., and Strosberg et al., have been discussed above, however none teach the use of an antibodies to other serotypes which can react with other serotypes. Jurgens et al., teaches cross-reacting lipopolysaccharide (LPS) antigens in *Legionella pneumophila* serotypes 1 to 14. The well characterized 24 kD surface protein Mip, has been found on all *L. pneumophila* serogroups, yet not on any other *Legionella species* (page 2180). "Antiserum prepared against serotype 5 was used to probe the LPS from *L. pneumophila* serogroups 1 to 14, the antibodies recognized a common epitope harbored by all *L. pneumophila* serogroups but not other *Legionella* species or by the gram-negative bacteria tested as controls" (abstract). The LPS is the serogroup specific antigen which is responsible for the diversity of serogroup 1 to 14 (page 2180).

Therefore, it would have been obvious at the time of applicants invention to have used antibodies from the known LPS antigen from serotype 5 which cross reacts with serotypes 1 to 14

as taught by Jurgens et al., with the well known method for detection of *Legionella* taught by Imrich et al., where the antibodies were purified using well known affinity chromatography techniques as taught by Cuatrecasas et al., in water samples as taught by Strosberg et al., because this antibodies reacts only with *L. pneumophila* serotypes and not with other *Legionella* species or other gram-negative bacteria.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al.(US Patent 5,415,994) in view of Cuatrecasas et al. (US Patent 4,411,832) in view of Strosberg et al (US Patent 4,780,407) and in further view of et al. Imrich et al.,Cuatrecasas et al., and Strosberg et al., have been discussed above, however none teach the use of an antibodies to other serotypes which can react with other serotypes.

Prior Art

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Barthe et al., teaches a common epitope on serotypes 1-8 located on the carbohydrate moiety of the lipopolysaccharide (LPS) of *Legionella pneumophila* which is recognized by a monoclonal antibody. Ciesielski et al., teaches serogroup specificity of Legionella pneumophila is related to LPS characteristics. Kazandijian et al., teaches rapid diagnosis of Legionella pneumophila serotype 1. Kohler et al.(US Patent 4,514,509) teaches methods for diagnosis of Legionaries' disease.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

February 6, 2001

2/8/01

JENNIFER GRASER
PATENT EXAMINER